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09/834,410	04/12/2001	Toyohiro Sawada	019941-000510US	3651

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	**PAPER NUMBER**
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/834,410	SAWADA ET AL.	
	Examiner	Art Unit	
	MICAH-PAUL YOUNG	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-7 and 13-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-7 and 13-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Response dated 7/9/08.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1, 3, 5-7, and 13-26 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 5-7 and 13-26 of copending Application No. 11/463,570 in view of Ullah et al (USPN 6,235,311 hereafter '311). The claims are drawn to a compression coated timed release formulation comprising a core comprising a drug and a filler, and an outer coating comprising polyethylene glycol and polyethylene oxide. The outer coating does not comprise the drug of the inner core. The claims of the '570 specify that the outer coating must comprise a drug, while the instant claims are open to there being no drug present or a different drug all together. This concept of separate drugs being present in the core and outer coatings is an obvious modification as is seen in the '311

patent, where the core comprises aspirin while the outer layer comprises a compound that counteracts the negative effects of the aspirin. It would have been obvious to modify the invention as such in order to provide a safer formulation as well as provide a combination therapy for wider treatment options.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1, 7, 14-17, 21, 22, 24, 25, and 27 rejected under 35 U.S.C. 103(a) as being unpatentable over Luber et al (USPN 6,277,409 hereafter '409). The claims are drawn to a timed release tablet comprising an inner core comprising a drug and filler, and an outer coating comprising polyethylene oxide and polyethylene glycol, where the drug is present in the outer layer.

6. The '409 patent discloses a tablet formulation comprising an inner core comprising a filler and an outer layer comprising a thermoplastic coating (abstract). The fillers in the core include sucrose, lactose, and the like (col. 3, lin. 3-8). The thermoplastic polymers include mixtures of polyethylene glycol and polyethylene oxide (col. 3, lin. 50-55). The drugs include decongestants, diuretics and sleep inducing agents and compounds that are metabolized by and/r inhibit the effect of cytochrome P-450 (col. 2, lin. 30-49). The outer layer does not contain the drug of the inner core (examples). The formulation comprises the same components of the instant claims and therefor would also release in the lower digestive tract, and alleviate drug interactions inherently.

7. Regarding the percentage erosion of the filler, it is the position of the Examiner that this percentage would be inherent to any filler meeting the limitations of the claims. Sucrose and lactose are named in the specification as capable and useful fillers, thus these filler, present in the prior art would act identically and erode to the given percentage. Applicant is invited to provide evidence as to how the sucrose of the instant claims would behave differently than the sucrose of the prior art. Further no temporal data is given regarding when or where the eroding takes place. Any filler will erode 40-90% given enough time in the digestive tract, regardless of coating and presentation.

8. Regarding the claim reciting the determination of the eroding percentage, it is the position of the Examiner that the limitations render the claim a product by process claim. The claim is drawn to a tablet, yet recited methods of determination. Also regarding the compression coated limitation, it is the position of the Examiner that such a limitation is merely a product by process limitation, describing the manner in which the tablet is formed. Applicant is reminded

that regarding product-by-process claims, even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

9. The reference is silent to the specific example showing polyethylene oxide and glycol combined into a singular coating layer, however provides sufficient suggestion and motivation to produce such as coating since both compounds are mentioned together and disclosed as possible coating combination.

10. With these things in mind it would have been obvious to follow the suggestions and teachings of the '410 patent in order to produce a stable controlled release formulation comprising an inner core and outer protective coating useful in alleviating drug interactions in combination therapy. One of ordinary skill in the art would have been able to arrive at the invention of the current claims with an expected result of a coated controlled release formulation releasable in the lower digestive tract.

11. Claims 1, 3, 5-7, and 13-26 rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Luber et al (USPN 6,277,409 hereafter '409) in view of Sako et al (EP 0 661 045 hereafter '045) and Taniguchi et al (EP 0 709 386 hereafter '386). The claims are drawn to a controlled release formulation comprising an inner core comprising a drug and fillers,

and an outer layer comprising a mixture of polymers, where the drug of the inner core is not present.

12. As discussed above the '409 patent discloses a coated tablet comprising fillers and a combination of water soluble and swellable polymers in the coating. The reference is however silent to the specific fillers, and active agents of the instant claims. These fillers are well known in the art as shown in the '045 patent. Likewise the active agents are well known as seen in the '386 patent.

13. The '045 reference teaches a compression molded oral formulation comprising a core comprising a drug (pg. 3, lin. 1-29), along with solubilizers that help improve the solubility of the drug in water such as citric acid, tartaric acid, and polyethylene glycol (pg 3, lin. 30-43). The core is coated with a hydrogel formulation comprising a hydrophilic base such as polyethylene glycols (pg. 3, lin. 49-pg. 4, lin. 7) and hydrogel-forming polymers with viscosities not less than 1000 cps in 1% aqueous solution such as polyethylene oxides (pg. 4, lin. 8-51). The formulation can include hydrogel-forming polymers in the core such as hydroxypropylmethylcellulose (pg. 3, lin. 37). The formulation further includes yellow iron sesquioxide (pg. 13, lin. 10-15). The drugs include lidocaine, nicardipine, and quindine, agents that are all metabolized by CYP3A4 (pg. 3, lin. 5-25). Upon administration, water is absorbed into the core of the formulation during its stay in the upper intestine, essentially dissolving the core and releasing the drug slowly as it travels to the colon (pg 2, lin. 35-40). The drug is present in the formulation in concentrations from 80-85%, the hydrophilic base is present in concentration from 5-80%, the hydrogel-forming polymer is present in concentration greater than 16% and solubilizing agent that aids in water absorption into the core is present in concentrations from 15-90% (pg. 3 lin. 25-pg. 5, lin. 13).

The formulation remains within the digestive tract for up to 12 hours and within that time the formulation dissolves 70-100% (figures). The reference establishes the level of skill in the art regarding specific fillers and their relation to compression coatings and hydrogel-forming compression tablets. The artisan of ordinary skill would have been able to include the fillers of the '045 reference into the '409 since both formulation disclose similar formulations.

14. The '386 patent discloses a fused benzazepine derivative, which can be useful as a vasopressin antagonist. The drug can be formulated into tablets using conventional excipients such as sucrose, gelatin and hydroxypropylcellulose (pg. 27, lin. 23 – 37). The drug of the invention can be used in the treatment of various disorders ranging from cerebrovascular disease to renal disorders (pg. 23, lin. 24 – 44). A skilled artisan would be able to include the compound of '386 into the formulation of '352 since the '352 reference uses similar drugs to treat similar disorders.

15. Regarding the specific concentrations recited in the claims, the '409 patent discloses the active agents present in varying concentrations. The active agents are from 90-95% of the coated granulation, approximately 27-38% of the total formulation. The '045 patent provides a coating similar to that of the '409 patent (a combination of polyethylene oxide and glycol) where the polymers are present in concentrations within the limits of the instant claims. It is the position of the Examiner that an artisan of ordinary skill would be motivated to coat the tablets of the '409 with the bilayered coating of the '045 in order to provide an improved controlled release of the inner active agents. The coating allows for water to penetrate into the core providing optimal release in the lower intestine. These concentrations allow for the optimal release and would result from routine experimentation. Where the general conditions of a claim are disclosed in the

prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

16. Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various pharmaceutical compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

17. With these thing in mind it would have been obvious to combine the prior art in order to provide a stable controlled release formulation with improved lower digestive tract release. Following the suggestions of the '409 patent to coat the core tablet with a mixture of polyethylene glycol and oxide, it would have been obvious to apply the coating of the '045 patent in order to provide proper release of the core active agents. It would have been obvious to substitute the active agent of the '386 patent into the combination. One of ordinary skill in the art would have been motivated to combine the suggestions and teachings of the prior art with an expected result of a stable controlled release formulation useful in alleviating undesirable drug interactions.

Response to Arguments

Applicant's arguments filed 7/9/08 have been fully considered but they are not persuasive. Applicant argues that;

> The Luber patent does not obviate the instant claims since the outer layer does not allow for the erosion of the core material.

The combination of the Luber, Sako and Taniguchi patents do not obviate the claims since the Luber patent fails to disclose the erosion of the core and the Sako and Taniguchi patents do not remedy this deficiency.

Regarding the Luber patent, it remains the position of the Examiner that the Luber patent obviates in the instant claims. Applicant argues that the Luber patent does not relate to a timed-release composition, however applicant is reminded that such a limitation is merely a future intended use that does not breathe life into the claim. Where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation. See also *Rowe v. Dror*, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997). The Luber patent discloses a coated formulation with a core, effectively meeting the structural limitations of the instant claims. Applicant further argues that the outer waxy coating would not allow for the core material to erode to the recited 40-90% required by the instant claims. First the outer protective coating is optional and not a requirement of the Luber invention. Regardless of the inclusion of the outer protective layer, applicant is reminded that the language of the instant claims is open and can further include other layers added to the coating. Applicant points to a disclosure in the Luber patent where an outer coating is added to prevent the core from eroding due to the coating materials. Meaning the core does not prematurely erode. Further the protective coating is made of water soluble polymers (claims). The claims do not recite that the coating allows for the core to erode, only that he core erodes in the digestive tract to a specific percentage, which is due tot he erodible fillers present in the core. Since the erodible fillers of the instant claims are also recited in the Luber patent (sucrose and lactose) it remains the position of the Examiner that such

erosion would still occur. Also **any** core will erode 40-90% given enough time in the digestive tract. With these things in mind, the Luber patent discloses a coated core where the core comprises the same erodible fillers and the instant claims and the coating comprises the same polymers as the instant claims. The instant claims are open to the inclusion of other ingredients including cores. And even if other layers are added the claims recite that the core erodes due to its erodible fillers not by the action of the polymer coating. The coating of the Luber patent does not contain the drug of the core and the core does not contain any of the hydrogel forming polymer of the coating. For the reasons the claims remain obviated.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, regarding the combination of the Luber patent with the Sako and Taniguchi patents, it remains the position of the Examiner that the combination continues to obviate the claims. As discussed above the Luber patent discloses a coated solid formulation comprising a core with erodible fillers and a polymeric coating comprising hydrogel forming polymers and a hydrophilic base. The Luber patent is silent to the specific fillers of the claims 5 and 6 and the specific combination of hydrogel forming polymers and hydrophilic base polymers. The Sako patent provides a compression molded formulation comprising the fillers of claims 5 and 6, where the core erodes along the path of the digestive system. The core portion of the tablet erodes from 70 -100%, gelling in the process. The Taniguchi patent establishes the level of skill in the art regarding the combination of benzazepine derivatives and their delivery as coated tablets where the core

comprise erodible fillers such as sucrose and gelatin. Applicant argues that these three patents are not related however the Luber patent discloses coated solid dosage forms where the core comprises erodible fillers, and the coating has a range of hydrophilic base polymers and hydrogel forming polymers. The Sako patent discloses a tablet comprising these hydrophilic base polymers and hydrogel forming polymers, where the core of the tablet comprises citric acid, and the core gels/erodes from 70-100% in the digestive system. The Taniguchi patent discloses coating tablet formulations where the cores comprise similar erodible fillers. Each of the patents provides a coated core portion where the core portion comprises erodible fillers. The Luber patent provides the core and coating structures, while the Sako and Taniguchi patent provide the disclosures to include specific polymers in the coating and the core, alone with auxiliary components such as coloring compounds. For these reasons the claims remain rejected.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICAH-PAUL YOUNG whose telephone number is (571)272-0608. The examiner can normally be reached on Monday-Friday 7:00-4:30; every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/MICAH-PAUL YOUNG/
Examiner, Art Unit 1618